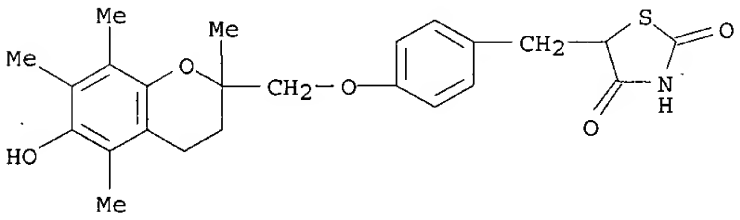
L96 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **97322-87-7** REGISTRY
CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 58: PN: WO0148150 SEQID: 73 claimed sequence
CN CI 991
CN CS 045
CN GR 92132X
CN Noscal
CN Rezulin
CN Romglizone
CN Troglitazone
FS 3D CONCORD
DR 259223-65-9
MF C24 H27 N O5 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

915 REFERENCES IN FILE CA (1962 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
924 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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L90  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   7440-47-3  REGISTRY
CN   Chromium (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Alpaste RRA 030
CN   Alpaste RRA 050
CN   Chrome
CN   Chromium element
DR   188785-87-7, 195161-82-1
MF   Cr
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES,
       DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, HSDB*,
       IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT,
       NIOSHTIC, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, ULIDAT,
       USPAT2, USPATFULL, VETU, VTB
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)


Cr

          151083 REFERENCES IN FILE CA (1962 TO DATE)
            5678 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          151249 REFERENCES IN FILE CAPLUS (1962 TO DATE)


=> s e44
L91           1 2295-31-0/BI

=> d


L91  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   2295-31-0  REGISTRY
CN   2,4-Thiazolidinedione (8CI, 9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2-Thiazolin-4-one, 2-hydroxy- (7CI)
CN   Thiazolidinedione (6CI)
OTHER NAMES:
CN   2,4(3H,5H)-Thiazoledione
CN   2,4-Dioxothiazolidine
CN   U 25560
FS   3D CONCORD
MF   C3 H3 N O2 S
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE, GMELIN*, HODOC*, IFICDB,
       IFIPAT, IFIUDB, MEDLINE, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER,
       USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, NDSL**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
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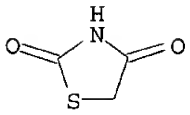


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

746 REFERENCES IN FILE CA (1962 TO DATE)
185 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
751 REFERENCES IN FILE CAPLUS (1962 TO DATE)
11 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

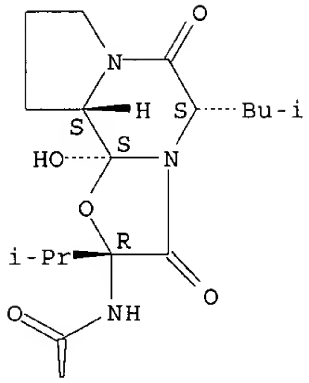
=> s e45
L92 1 25614-03-3/BI

=> d

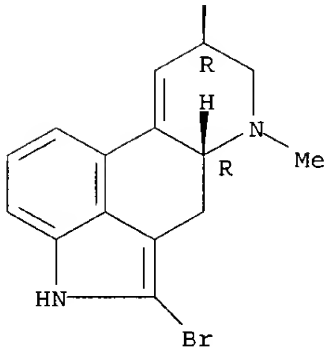
L92 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **25614-03-3** REGISTRY
CN Ergotaman-3',6',18-trione, 2-bromo-12'-hydroxy-2'-(1-methylethyl)-5'-(2-methylpropyl)-, (5'.alpha.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 8H-Oxazolo[3,2-a]pyrrolo[2,1-c]pyrazine, ergotaman-3',6',18-trione deriv.
CN Ergocryptine, 2-bromo- (8CI)
CN Indolo[4,3-fg]quinoline, ergotaman-3',6',18-trione deriv.
OTHER NAMES:
CN .alpha.-Bromoergocryptine
CN 2-Bromo-.alpha.-ergocryptine
CN 2-Bromo-.alpha.-ergokryptine
CN 2-Bromoergocryptine
CN Bromergocryptine
CN Bromocriptin
CN Bromocriptine
CN Bromocryptine
CN Bromoergocryptine
CN SAN 15-754
CN Sandoz 15-754
FS STEREOSEARCH
DR 127931-09-3, 148043-11-2, 26409-15-4, 47830-26-2
MF C32 H40 Br N5 O5
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGPAT, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

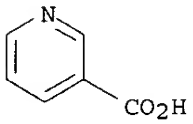
2267 REFERENCES IN FILE CA (1962 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2267 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> s e46
L93 1 59-67-6/BI

=> d

L93 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **59-67-6** REGISTRY
CN 3-Pyridinecarboxylic acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Nicotinic acid (7CI, 8CI)

OTHER NAMES:
CN .beta.-Pyridinecarboxylic acid
CN 3-Carboxylpyridine
CN 3-Carboxypyridine
CN 3-Pyridylcarboxylic acid
CN Akotin
CN Apelagrin
CN Daskil
CN Efacin
CN Enduracin
CN Linic
CN Niac
CN Niacin
CN Niacor
CN Niaspan
CN Nicacid
CN Nicangin
CN Nico-Span
CN Nicobid
CN Nicodelmine
CN Nicolar
CN Niconacid
CN Nicosan 3
CN Nicotinipca
CN Nicyl
CN Nyclin
CN Pellagrin
CN Pelonin
CN Slo-niacin
CN SR 4390
CN Wampocap
FS 3D CONCORD
DR 123574-58-3
MF C6 H5 N O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10107 REFERENCES IN FILE CA (1962 TO DATE)
493 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10146 REFERENCES IN FILE CAPLUS (1962 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L94           1 61912-98-9/BI

=> d

L94  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   61912-98-9  REGISTRY
CN   Insulin-like growth factor (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   IGF
CN   Insulin, -like activity
CN   Insulin-like activity, nonsuppressible
CN   Nonsuppressible insulin-like activity
CN   Nonsuppressible insulin-like growth factor
MF   Unspecified
CI   PMS, COM, MAN
PCT  Manual registration
LC   STN Files:   ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
       CAPLUS, CEN, CHEMCATS, CIN, EMBASE, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             2019 REFERENCES IN FILE CA (1962 TO DATE)
               67 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             2029 REFERENCES IN FILE CAPLUS (1962 TO DATE)


=> s e48
L95           1 9004-10-8/BI

=> d

L95  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2003 ACS
RN   9004-10-8  REGISTRY
CN   Insulin (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Actrapid
CN   Actrapid HM
CN   Actrapid MC
CN   Decurvon
CN   Dermulin
CN   Endopancrine
CN   Exubera
CN   HMR 4006
CN   Iletin
CN   Insular
CN   Insulin Injection
CN   Insulyl
CN   Intesulin B
CN   Iszilin
CN   Musulin
DR   8049-67-0, 8049-95-4, 9004-12-0, 9045-63-0, 9045-65-2, 9045-66-3,
     9045-67-4, 9066-39-1, 9066-40-4, 11081-38-2, 57126-42-8, 37243-75-7,
     37294-43-2, 69090-47-7, 88026-11-3, 88026-12-4
MF   Unspecified
CI   PMS, COM, MAN
PCT  Manual registration
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
       CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM,
       CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA,
       MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PHARMASEARCH, PIRA,
       PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VTB
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**, WHO
         (**Enter CHEMLIST File for up-to-date regulatory information)
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

82026 REFERENCES IN FILE CA (1962 TO DATE)

1503 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

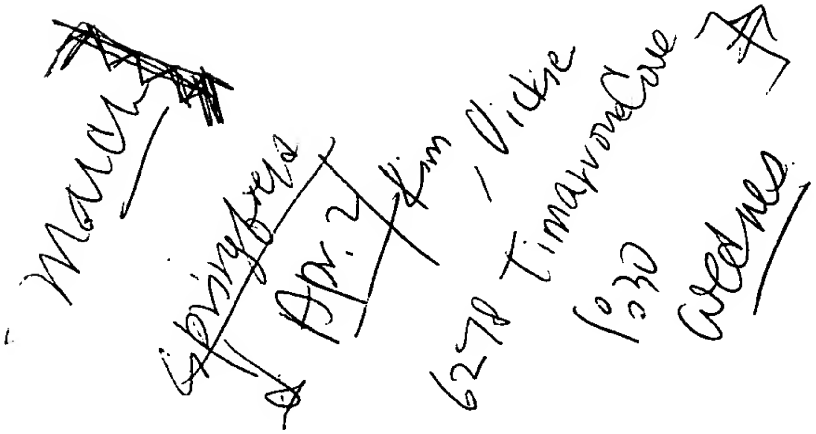
82089 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L18 ANSWER 54 OF 63 USPATFULL

AB Modified starch materials having a number average molecular weight of at least 10,000 for nutritional products provide a relatively slow release of **metabolizable carbohydrates**, giving a source of carbohydrate energy over a longer period of time than can be obtained from glucose and other carbohydrates such as lactose, fructose, or sucrose.

ACCESSION NUMBER:	97:114971 USPATFULL
TITLE:	Nutritional products containing modified starches
INVENTOR(S):	Sharp, Rickey L., Woodland Park, CO, United States Robyt, John F., Ames, IA, United States Kaplan, Murray L., Ames, IA, United States
PATENT ASSIGNEE(S):	Iowa State University Research Foundation, Inc., Ames, IA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5695803		19971209	
APPLICATION INFO.:	US 1995-465884		19950606	(8)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Czaja, Donald E.			
ASSISTANT EXAMINER:	Koh, C			



L31 ANSWER 20 OF 26 USPATFULL

DETD The invention further contemplates that the inhibitors of AGE-formation can be administered in conjunction with other therapies for the treatment of diseases that involve amyloidosis. For example, for treatment of a neurodegenerative disease, in particular **Alzheimer**'s disease, an inhibitor of AGE-formation can be administered in conjunction with a therapy designed to inhibit production of .beta.AP, such as those described by Gandy et al., U.S. Pat. No. 5,242,932, issued Sep. 7, 1993; Wagner et al., International Pat. Publication No. WO 93/09233, published May 13, 1993; and Buxbaum et al., European Pat. Publication No. 0457295 A2, published Nov. 21, 1991. In another example, for treatment of Type II diabetes, administration of an inhibitor of AGE-formation can be effected in conjunction with administration of one or more of sulfonylureas (drugs to increase the level of **insulin** production), **insulin**, hypertension medication, and imposition of a **diet** and exercise regimen.

ACCESSION NUMBER: 1999:92643 USPATFULL

TITLE: Compositions and methods for stimulating amyloid removal in amyloidogenic diseases using advanced glycosylation endproducts

INVENTOR(S): Vitek, Michael P., East Norwich, NY, United States
Cerami, Anthony, Shelter Island, NY, United States
Bucala, Richard J., New York, NY, United States
Ulrich, Peter C., Old Tappan, NJ, United States
Vlassara, Helen, Shelter Island, NJ, U

L31 ANSWER 20 OF 26 USPATFULL

DETD The invention further contemplates that the inhibitors of AGE-formation can be administered in conjunction with other therapies for the treatment of diseases that involve amyloidosis. For example, for treatment of a neurodegenerative disease, in particular **Alzheimer**'s disease, an inhibitor of AGE-formation can be administered in conjunction with a therapy designed to inhibit production of .beta.AP, such as those described by Gandy et al., U.S. Pat. No. 5,242,932, issued Sep. 7, 1993; Wagner et al., International Pat. Publication No. WO 93/09233, published May 13, 1993; and Buxbaum et al., European Pat. Publication No. 0457295 A2, published Nov. 21, 1991. In another example, for treatment of Type II diabetes, administration of an inhibitor of AGE-formation can be effected in conjunction with administration of one or more of sulfonylureas (drugs to increase the level of **insulin** production), **insulin**, hypertension medication, and imposition of a **diet** and exercise regimen.

ACCESSION NUMBER: 1999:92643 USPATFULL

TITLE: Compositions and methods for stimulating amyloid removal in amyloidogenic diseases using advanced glycosylation endproducts

INVENTOR(S): Vitek, Michael P., East Norwich, NY, United States
Cerami, Anthony, Shelter Island, NY, United States
Bucala, Richard J., New York, NY, United States
Ulrich, Peter C., Old Tappan, NJ, United States
Vlassara, Helen, Shelter Island, NJ, United States
Zhang, Xini, Jericho, NJ, United States

PATENT ASSIGNEE(S): The Picower Institute For Medical Research, Manhasset, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5935927		19990810	
	WO 9520979		19950810	
APPLICATION INFO.:	US 1996-501127		19960810	(8)
	WO 1995-US1380		1995	

L61 ANSWER 7 OF 204 CAPLUS COPYRIGHT 2003 ACS
AN 1995:887989 CAPLUS
DN 123:276079
TI Compositions and methods for advanced glycosylation endproduct-mediated modulation of amyloidosis
IN Vitek, Michael P.; Cerami, Anthony; Bucala, Richard J.; Ulrich, Peter C.; Vlassara, Helen; Zhang, Xini
PA Picower Institute for Medical Research, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K039-395
ICS A61K031-155; A61K031-195; A61K031-425; A61K031-655; C07K014-575; C07K014-47; G01N033-68
CC 1-12 (Pharmacology)
Section cross-reference(s): 33
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9520979	A1	19950810	WO 1995-US1380	19950202
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2182731	AA	19950810	CA 1995-2182731	19950202
	AU 9518701	A1	19950821	AU 1995-18701	19950202
	AU 692237	B2	19980604		
	EP 802797	A1	19971029	EP 1995-910911	19950202
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT				
	JP 09511492	T2	19971118	JP 1995-520751	19950202
	US 6410598	B1	20020625	US 1995-477364	19950607
	US 5935927	A	19990810	US 1996-501127	19960810
PRAI	US 1994-191579	A	19940203		
	US 1994-311768	A	19940923		
	WO 1995-US1380	W	19950202		
	US 1995-457169	A2	19950601		

OS MARPAT 123:276079
AB The present invention relates generally to the nonenzymic glycosylation of amyloidogenic proteins and the consequent formation of advanced glycosylation endproducts (AGEs). It has been found that formation of AGE-amyloidogenic proteins can enhance amyloidosis. The invention further relates to compns. and methods for the prevention and treatment of amyloidosis assocd. with amyloid diseases, particularly neurodegenerative disease and Type II diabetes, and more particularly **Alzheimer**"s disease. In a specific example, aggregation of an amyloidogenic peptide, .beta.-AP, is enhanced by the glycosylation reaction of .beta.-AP to form AGE-.beta.-AP as defined herein. Accordingly, the invention extends to a method for modulating the in vivo aggregation of amyloid polypeptides and assocd. amyloidosis by controlling the formation and presence of AGE-amyloid polypeptide. A corresponding diagnostic utility comprises the measurement of the course and extent of amyloidosis by a measurement of the presence and amt. of AGEs and particularly, AGE-amyloid. An assay is included that may use the AGE-amyloid polypeptide of the present invention to identify disease states characterized by the presence of AGE-amyloid. Addnl., such an assay can be utilized to monitor therapy and thus adjust a dosage regimen for a given disease state characterized by the presence of AGE-amyloid. Prepn. of AGE-thioflavins is also described. Binding to amyloid of a thioflavin T-amadori product was demonstrated.
ST amyloidosis advanced glycosylation endproduct amyloidogenic protein; AGE

amyloidogenic protein amyloidosis treatment diagnosis

IT Pancreas
(AGE-amylin-mediated amyloidosis prevention in; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Blood analysis
Cerebrospinal fluid
Peritoneal fluid
Urine analysis
(AGE-amyloid polypeptide detection in; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Ligands
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(advanced glycosylation endproduct-binding or -neutralizing; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Amyloidosis
Blood-brain barrier
Down's syndrome
Macrophage
Monocyte
Nervous system agents
Phagocyte
(advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Antidiabetics and Hypoglycemics
(for type II diabetes; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to advanced glycosylation endproducts; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Amyloids
RL: ANT (Analyte); ANST (Analytical study)
(A, advanced glycosylation endproduct-; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AGE (advanced glycosylation end product), advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Glycoprotein receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AGE (advanced glycosylation end product), advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Mental disorder
(**Alzheimer**'s disease, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Brain, disease
(Creutzfeldt-Jakob, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Parkinsonism
(Guamanian parkinsonism-dementia, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Glycolipoproteins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(PrP (prion protein), advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Proteins, specific or class
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(amyloid A4, advanced glycosylation endproduct-; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(amyloid A4, pre-, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Brain, disease
(amyloid angiopathy, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Blood vessel, disease
(amyloid angiopathy, asymptomatic; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(amyloidogenic, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Nervous system
(disease, Gerstmann-Straussler syndrome, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Nervous system
(disease, degeneration, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Nervous system
(disease, kuru, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Nervous system
(disease, scrapie, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Receptors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycoprotein AGE, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Amyloidosis
(hereditary, cerebral hemorrhage type, Dutch type, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT **Carbohydrates** and Sugars, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**reducing**, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT Brain, disease
(spongiform encephalopathy, advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT 106602-62-4, Amylin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(advanced glycosylation endproduct-; advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT 169553-21-3P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT 50-69-1, Ribose 50-99-7, Glucose, biological studies 56-73-5, Glucose-6-phosphate 57-48-7, Fructose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT 92-36-4, 2-(4-Aminophenyl)-6-methylbenzothiazole 5394-18-3, N-(4-Bromobutyl)phthalimide 7803-57-8, Hydrazine hydrate 32315-10-9, Bis(trichloromethyl) carbonate 32786-02-0 51857-17-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(advanced glycosylation endproduct-mediated modulation of amyloidosis)

IT 67229-93-0P 169553-13-3P 169553-14-4P 169553-16-6P 169553-17-7P 169553-18-8P 169553-20-2P
RL: RCT (Reactant); SPN (Synthetic preparat

brand drug (Hoechst-Roussel). GLUCOTROL.TM. (Pratt) is the trademark for a glipizide (1-cyclohexyl-3-(p-(2-(5-methylpyrazine carboxamide)ethyl)phenyl)sulfonyl)urea) tablet available in both 5- and 10-mg strengths and is also prescribed to Type II diabetics who require hypoglycemic therapy following dietary control or to patients who have ceased to respond to other sulfonylureas. Physician's Desk Reference, 1902-1903 (1995). Other hypoglycemic agents than sulfonylureas, such as the biguanides (e.g., metformin and phenformin) or thiazolidinediones (e.g., troglitozone), or other drugs affecting insulin action may also be employed. If a thiazolidinedione is employed with the compound, it is used at the same level as currently used or at somewhat lower levels, which can be adjusted for effects seen with the compound alone or together with the dione. The typical dose of **troglitazone** (REZULIN.TM.) employed by itself is about 100-1000 mg per day, more preferably 200-800 mg/day, and this range is applicable herein. See, for example, Ghazzi et al., Diabetes, 46: 433-439 (1997). Other thiazolidinediones that are stronger insulin-sensitizing agents than **troglitazone** would be employed in lower doses.

ACCESSION NUMBER: 2000:125192 USPATFULL
TITLE: Insulin-like growth factor agonist molecules
INVENTOR(S): Clark, Ross G., Pacifica, CA, United States
Lowman, Henry B., El Granada, CA, United States
Robinson, Iain C. A. F., St. Albans, United Kingdom
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6121416		20000919	
APPLICATION INFO.:	US 1997-825852		19970404	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kemmerer, Elizabeth
ASSISTANT EXAMINER: Romeo, David S.
LEGAL REPRESENTATIVE: Hasak, Janet E.
NUMBER OF CL

the like in order to lower plasma levels of leucine, isoleucine and valine which would otherwise compete for brain uptake.

CLM What is claimed is:

1. The process for relieving the adverse effects of neurological disease or aging in a patient which comprises administering to said patient a composition consisting essentially of (a) an amino acid selected from the group consisting of phenylalanine, tyrosine, threonine, tryptophan, and mixtures thereof in an amount to increase release in the brain of said patient of a neurotransmitter produced from said amino acid (b) an amount of a compound effective to raise the bloodstream choline level of a patient to between about 10 and 50 nanomoles/ml and to release adequate amounts of brain acetylchlorine selected from the group consisting of choline, a choline salt, a choline ester, sphingomyelin, cytidine-diphospho-choline and an acylglycerophosphocholine of the formula: ##STR2## wherein FA.sub.1 and FA.sub.2 can be the same or different and are fatty acid residues having from 6-26 atoms, and mixtures thereof, and (c) an insulin-releasing **carbohydrate**.

9. A composition of matter consisting essentially of (a) an amino acid selected form the group consisting of phenylalanine, tyrosine, threonine, tryptophan and mixtures thereof in an amount to increase release in the brain of a patient of a neurotransmitter produced from said amino acid, (b) an amount of a compound effective to raise the bloodstream choline level of a patient to between about 10 and 50 nanomoles/ml and to release adequate amounts of brain acetylcholine selected from the group consisting of choline, a choline salt, a choline ester, sphingomyelin, cytidine-diphospho-choline and an acylglycerophosphocholine of the formula: ##STR3## wherein FA.sub.1 and FA.sub.2 can be the same or different and are fatty acid residues having from 6-26 carbon atoms, and mixtures thereof and (c) and insulin releasing **carbohydrate**.

IN Wurtman, Richard J., Boston, MA, United States
TI Method and composition for treating neurological disorders and aging|
PI US 4775665 19881004

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L51 ANSWER 38 OF 53 USPATFULL

SUMM [0006] Current pharmacological therapies for type 2 DM include injected insulin, and oral agents that are designed to lower blood glucose levels. Currently available oral agents include (i) the sulfonylureas, which act by enhancing the sensitivity of the pancreatic beta cell to glucose, thereby increasing insulin secretion in response to a given glucose load; (ii) the biguanides, which improve glucose disposal rates and inhibit hepatic glucose output; (iii) the thiazolidinediones, which improve peripheral **insulin sensitivity** through interaction with nuclear peroxisome proliferator-activated receptors (PPAR, see, e.g., Spiegelman, 1998 Diabetes 47:507-514; Schoonjans et al., 1997 Curr. Opin. Lipidol. 8:159-166; Staels et al., 1997 Biochimie 79:95-99), (iv) repaglinide, which enhances insulin secretion through interaction with ATP-dependent potassium channels; and (v) acarbose, which decreases intestinal absorption of **carbohydrates**. Although currently available drugs for **treating** type 2 diabetes, such as the sulfonylureas, improve insulin secretion, both basal and insulin stimulated insulin secretion are enhanced by such compounds. Consequently, undesirable chronic hyperinsulinemia, hypoglycemia and/or excessive weight gain may result following **treatment** with such drugs (Cobb et al., 1998 Ann. Rep. Med. Chem. 33:213-222; Krentz et al., 1994 Drug Safety 11:223-241).

ACCESSION NUMBER: 2002:157589 USPATFULL
TITLE: Inhibition of mitochondrial calcium/sodium antiporter
INVENTOR(S): Anderson, Christen M., Encinitas, CA, UNITED STATES
Davis, Robert E., San Diego, CA, UNITED STATES
Pei, Yazhong, San Diego, CA, UNITED STATES
Ghosh, Soumitra S., San Diego, CA, UNITED STATES
PATENT ASSIGNEE(S): MitoKor, San Diego, CA (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002082193	A1	20020627	
APPLICATION INFO.:	US 2001-960612	A1	20010920	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-233925P	20000920 (60)
	US 2000-256001P	20001215 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, SEATTLE, WA, 98104-7092
NUMBER OF CLAIMS: 40
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1991
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L113 ANSWER 35 OF 43 USPATFULL

ACCESSION NUMBER: 2001:82768 USPATFULL

TITLE: 1,2,4-benzothiadiazine derivatives, their preparation and use

INVENTOR(S): Pirotte, Bernard, Oupeye, Belgium
Lebrun, Philippe, Bruxelles, Belgium
De Tullio, Pascal, Liege, Belgium
Somers, Fabian, Liege, Belgium
Delarge, Jacques, Delembreux, Belgium
Hansen, John Bondo, Jyderup, Denmark
Nielsen, Flemming Elmelund, Virum, Denmark
Hansen, Holger Claus, V.ae butted.rl.o slashed.se, Denmark
Mogensen, John Patrick, Vanl.o slashed.se, Denmark
M.o slashed.ller-Tagmose, Tina, Farum, Denmark

PATENT ASSIGNEE(S): Novo Nordisk AIS, Bagsvaerd, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6242443	B1	20010605	
APPLICATION INFO.:	US 1997-877456		19970617	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1996-693	19960621
	DK 1996-1451	19961219

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ford, John M.
LEGAL REPRESENTATIVE: Zelson, Esq., Steve T., Rozek, Esq., Carol E.
NUMBER OF CLAIMS: 55
EXEMPLARY CLAIM: 1
LINE COUNT: 2833

L113 ANSWER 35 OF 43 USPATFULL

SUMM By acting on potassium channels of the central nervous system these compounds can be used for treatment of various neurological and psychiatric diseases such as **Alzheimer**, epilepsia and cerebral ischemia.

SUMM Compounds of the present invention, which inhibit insulin secretion by activating potassium channels of the beta-cell can be used in combination with compounds which reduce blood glucose levels. Examples of such compounds are insulin, **insulin sensitizers**, such as **thiazolidinediones**, insulin secretagogues, such as repaglinide, tolbutamide, glibenclamide and glucagon like peptide (GLP1), inhibitors of .alpha.-glucosidases and hepatic enzymes responsible for the biosynthesis of glucose, and glucagon.

ACCESSION NUMBER: 2001:82768 USPATFULL
TITLE: 1,2,4-benzothiadiazine derivatives, their preparation and use
INVENTOR(S): Pirotte, Bernard, Oupeye, Belgium
Lebrun, Philippe, Bruxelles, Belgium
De Tullio, Pascal, Liege, Belgium
Somers, Fabian, Liege, Belgium
Delarge, Jacques, Delembreux, Belgium
Hansen, John Bondo, Jyderup, Denmark
Nielsen, Flemming Elmelund, Virum, Denmark
Hansen, Holger Claus, V.ae butted.rl.o slashed.se, Denmark
Mogensen, John Patrick, Vanl.o slashed.se, Denmark
M.o slashed.ller-Tagmose, Tina, Farum, Denmark
PATENT ASSIGNEE(S): Novo Nordisk AIS, Bagsvaerd, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6242443	B1	20010605	
APPLICATION INFO.:	US 1997-877456		19970617	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1996-693	19960621
	DK 1996-1451	19961219

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Ford, John M.
LEGAL REPRESENTATIVE: Zelson, Esq., Steve T., Rozek, Esq., Carol E.
NUMBER OF CLAIMS: 55
EXEMPLARY CLAIM: 1
LINE COUNT: 2833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L113 ANSWER 36 OF 43 USPATFULL

SUMM Potassium channel openers are also able to relax urinary bladder smooth muscle and therefore, can be used for the treatment of urinary incontinence. Potassium channel openers which relax smooth muscle of the uterus can be used for treatment of premature labor. By acting on potassium channels of the central nervous system these compounds can be used for treatment of various neurological and psychiatric diseases such as **Alzheimer**, epilepsia and cerebral ischemia.

SUMM Compounds of the present invention, which inhibit insulin secretion by activating potassium channels of the beta-cell can be used in combination with other compounds which may be used to treat non-insulin dependent diabetes mellitus and insulin dependent diabetes mellitus. Examples of such compounds are insulin, **insulin sensitizers**, such as **thiazolidinediones**, insulin secretagogues, such as repaglinide, tolbutamide, glibenclamide and glucagon like peptide (GLP1), inhibitors of .alpha.-glucosidases and hepatic enzymes responsible for the biosynthesis of glucose.

ACCESSION NUMBER: 2001:63687 USPATFULL
TITLE: Fused 1,2,4-thiadiazine derivatives, their preparation and use
INVENTOR(S): Nielsen, Flemming Elmelund, Virum, Denmark
Hansen, John Bondo, Jyderup, Denmark
Hansen, Holger Claus, Vaerlose, Denmark
Tagmose, Tina M.o slashed.ller, Ballerup, Denmark
Mogensen, John Patrick, Vanlose, Denmark
PATENT ASSIGNEE(S): Novo Nordisk A/S, Bagsvaerd, Denmark (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6225310	B1	20010501
APPLICATION INFO.:	US 2000-539242		20000330 (9)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1998-107693, filed on 30 Jun 1998, now abandoned Continuation-in-part of Ser. No. US 1997-785438, filed on 17 Jan 1997, now patented, Pat. No. US 5889002

	NUMBER	DATE
PRIORITY INFORMATION:	DK 1996-41	19960117
	DK 1996-250	19960305
	DK 1996-251	19960305
	DK 1996-252	19960305
	DK 1996-253	19960305
	DK 1996-256	19960305
	DK 1996-259	19960305
	DK 1996-903	19960827
	DK 1997-872	19970716
	DK 1998-368	19980317

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Shah, Mukund J.
ASSISTANT EXAMINER: Liu, Hong
LEGAL REPRESENTATIVE: Zelson, Esq., Steve T., Rozek, Esq., Carol E.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
LINE COUNT: 1719
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 65 OF 73 CAPLUS COPYRIGHT 2003 ACS
AN 1991:95474 CAPLUS
DN 114:95474
TI Characterization of insulin receptor kinase activity and autophosphorylation in different skeletal muscle types
AU Azhar, Salman; Butte, John C.; Santos, Rosa F.; Mondon, Carl E.; Reaven, Gerald M.
CS Sch. Med., Stanford Univ., Palo Alto, CA, 94305, USA
SO American Journal of Physiology (1991), 260(1, Pt. 1), E1-E7
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English
CC 2-6 (Mammalian Hormones)
AB Insulin binding, autophosphorylation, and tyrosine kinase activity was examd. in detergent-solubilized and wheat germ agglutinin-purified insulin receptor prepns. from 4 rat muscles of different fiber compn. (i.e., tensor fascia latae, soleus, vastus intermedius, and plantaris). Insulin binding activity was similar in 3 of the 4 muscles but lower in tensor fascia latae. No differences were noted in the affinity of insulin for its receptor from various muscle types. Insulin receptor **tyrosine** kinase activity measured in the absence (basal) and presence of insulin (0.3-300 nM) was comparable in all muscle types (normalized to the amt. of insulin bound). **Insulin sensitivity**, measured as the dose of insulin required for half-maximal activation of kinase activity, was also similar in all muscle types. Likewise, incubation of receptor prepns. with [.gamma.-32P]ATP, Mn2+, and insulin (0.25-100 nM) resulted in a dose-dependent autophosphorylation of the .beta.-subunit (relative mol. wt. .apprx.95 kDa) with similar kinetics in all muscle types. Thus, the functional behavior of the insulin receptor autophosphorylation-kinase system (in vitro) is not changed by alterations in muscle fiber compn., indicating that differences in insulin sensitivity between different skeletal muscle types is probably not due to modulation of the insulin receptor phosphorylation system.
ST insulin receptor kinase muscle type; phosphorylation auto insulin receptor muscle
IT Receptors

L17 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2003 ACS
AN 1998:80638 CAPLUS
DN 128:165872
TI Cerebrospinal fluid and plasma **insulin levels** in **Alzheimer**'s disease. Relationship to severity of dementia and apolipoprotein E genotype
AU Craft, Suzanne; Peskind, Elaine; Schwartz, Michael W.; Schellenberg, Gerard D.; Raskind, Murray; Porte, Daniel, Jr.
CS Geriatric Research, Education, and Clinical Center, VA Puget Sound Health Care System, Seattle, WA, 98108, USA
SO Neurology (1998), 50(1), 164-168
CODEN: NEURAI; ISSN: 0028-3878
PB Lippincott-Raven Publishers
DT Journal
LA English
CC 14-10 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
AB Patients with **Alzheimer**'s disease (AD) have elevations of fasting plasma insulin that are hypothesized to be assocd. with disrupted brain insulin metab. We examd. paired fasted plasma and CSF **insulin levels** in 25 patients with AD and 14 healthy age-matched adults and detd. whether **insulin levels** were related to severity of dementia and apolipoprotein E-.vepsiln. homozygosity, a known genetic risk factor for AD. The AD patients had lower CSF insulin, higher plasma insulin, and a reduced CSF-to-plasma insulin ratio when compared with healthy adults. The differences were greater for patients with more advanced AD. Patients who were not apolipoprotein E-.vepsiln.4 homozygotes had higher plasma insulin levels and reduced CSF-to-plasma ratios, whereas .vepsiln. homozygotes with AD had normal values. Both plasma and CSF insulin levels are abnormal in AD, and there are metabolic differences among apolipoprotein E genotypes.
ST Alzheimer insulin plasma cerebrospinal fluid apolipoprotein
IT Apolipoproteins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(E4; insulin in human cerebrospinal fluid and plasma in Alzheimer's disease in relation to severity of dementia and apolipoprotein E genotype)
IT Apolipoproteins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(E; insulin in human cerebrospinal fluid and plasma in Alzheimer's disease in relation to severity of dementia and apolipoprotein E genotype)
IT Mental disorder
(dementia; insulin in human cerebrospinal fluid and plasma in Alzheimer's disease in relation to severity of dementia and apolipoprotein E genotype)
IT Alzheimer's disease
Blood plasma
Cerebrospinal fluid
Genotypes
(insulin in human cerebrospinal fluid and plasma in Alzheimer's disease in relation to severity of dementia and apolipoprotein E genotype)
IT 9004-10-8, Insulin, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(insulin in human cerebrospinal fluid and plasma in Alzheimer's disease in relation to severity of dementia and apolipoprotein E genotype)

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L41 ANSWER 28 OF 32 USPATFULL

SUMM . . . disturbed oral glucose tolerance increases parallel to these hormonal changes. Examples of this are the various forms of diabetes mellitus, **high** blood pressure, hypercholesterolaemia and other disorders of the lipid or lipoprotein metabolism, myocardial infarction, and **Alzheimer**'s disease (Vermeulen A (1991): J. Clin Endocrinol Metab 73: 222). Quite frequently, the so-called metabolic syndrome is found in overweight elderly men which is accompanied by obesity, **insulin** or **insulin** receptor resistance, a testosterone deficit and a disproportionately **high** risk of cardiovascular diseases. There is a considerably increased mortality caused by cerebral or coronary ischaemia (McGovern PG et al.. . .

ACCESSION NUMBER: 1999:1247 USPATFULL

TITLE: Compound preparation for the treatment of hypogonadal men and men with hypophyseal diseases

INVENTOR(S): Oettel, Michael, Jena, Germany, Federal Republic of
Golbs, Siegfried, Leipzig, Germany, Federal Republic of
Dittgen, Michael, Apolda, Germany, Federal Republic of
Timpe, Carsten, Apolda, Germany, Federal Republic of
Graser, Thomas, Erfurt, Germany, Federal Republic of
Hubler, Doris, Schmieden, Germany, Federal Republic of

PATENT ASSIGNEE(S): Jenapharm GmbH & Co. KG, Jena, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5855905		19990105	
APPLICATION INFO.:	US 1997-841719		19970430	(8)

L41 ANSWER 23 OF 32 USPATFULL

DETD . . . transporters will allow more glucose to enter the cells located in the cortex cell layer I-III of the brain. In **Alzheimer** Disease where cortisol level is **high** in the CSF, the effect of cortisol is opposite that of **insulin**. Cortisol desensitizes the **insulin** receptors thereby unabling it to bind with **insulin**. Because the **insulin** can not bind to the receptor, additional glucose transporters are not transcribed at the cell membrane thereby causing a low. . . cells located in the cortex cell layer I-III and possibly cortex layer IV of the brain, a phenomena observed in **Alzheimer** disease. This observation of low glucose concentration in the cortex cell layer I-III and high level of cortisol in the. . .

DETD [0046] The following is an example that demonstrate the need of a medication or mode of treatment described above. In **Alzheimer** 's disease, the cortisol concentration in CSF is high while some neuropeptides will test lower than or higher than normal. Because of this **high** level of cortisol in the CSF, the beta-amyloid precursor (protein beta APP), and the tau protein found in the enthorhinal cortex layer II-IV are non functional. This phenomena can be explained by the alternate glucose pathway and the **insulin** pathway because the elevated cortisol depresses or makes unavailable the required glucose by the brain. This reduced glucose level results. . .

ACCESSION NUMBER: 2001:217984 USPATFULL

TITLE: Diagnoses and treatment of disorders using an alternative glucose pathway

INVENTOR(S): Morita, Kieko, Van Nuys, CA, United States

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2001046470	A1	20011129	
APPLICATION INFO.:	US 2001-854298	A1	20010509	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-202967P	20000510	(60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Maria Erlinda C. Sarno, Esq., P.O. Box 1023, Artesia, CA, 90702

NUMBER OF CLAIMS: 27

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 2 Drawing Page(s)

LINE COUNT: 653

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6316038	B1	20011113
APPLICATION INFO.:	US 1999-397109		19990916 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. WO 1998-GB5072, filed on 17 Mar 1998		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-40858P	19970317 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Reamer, James H.
LEGAL REPRESENTATIVE: Nixon & Vanderhye
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 1821
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [0020] The body normally produces small amounts of ketone bodies. However, because they are rapidly utilized, the concentration of ketone bodies in the blood is very low. Blood ketone body concentrations rise on a **low carbohydrate diet**, during periods of fasting, and in diabetics. In a **low carbohydrate diet**, blood glucose levels are low, and pancreatic insulin secretion is not stimulated. This triggers the oxidation of fatty acids for use as a fuel source when glucose is limiting. Similarly, during fasting or starvation, liver glycogen stores are quickly depleted, and fat is mobilized in the form of ketone bodies. Since both a **low carbohydrate diet** and fasting do not result in a rapid drop of blood glucose levels, the body has time to increase blood ketone levels. The rise in blood ketone bodies provides the brain with an alternative fuel source, and no cellular damage occurs. Since the brain has such high energy demands, the liver oxidizes large amounts of fatty acids until the body becomes literally saturated in ketone bodies. Therefore, when an insufficient source of ketone bodies is coupled with poor glucose utilization severe damage to neurons results. Since glial cells are able to utilize a large variety of substrates they are less susceptible to defects in glucose metabolism than are neurons. This is consistent with the observation that glial cells do not degenerate and die in AD (Mattson, 1998).

SUMM [0021] As discussed in the Metabolism and **Alzheimer**'s Disease section, in AD, neurons of the brain are unable to utilize glucose and begin to starve to death. Since the defects are limited to the brain and peripheral glucose metabolism is normal, the body does not increase production of ketone bodies, therefore neurons of the brain slowly starve to death. Accordingly, there remains a need for an energy source for brain cells that exhibit compromised glucose metabolism in AD patients. Compromised glucose metabolism is a hallmark of AD; hence administration of such an agent will prove beneficial to those suffering from AD.

SUMM [0025] Numerous patents relate to use of MCT. None of these patents relate to the specific use of MCT for treatment and prevention of **Alzheimer**'s Disease. Patents such as U.S. Pat. No. 4,528,197 "Controlled triglyceride nutrition for hypercatabolic mammals" and U.S. Pat. No. 4,847,296 "Triglyceride preparations for the prevention of catabolism" relate to the use of MCT to prevent body-wide catabolism that occurs in burns and other serious injuries. Each patent described herein is incorporated by reference herein in its entirety.

SUMM [0026] The present invention provides a method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of medium chain triglycerides to a patient in need thereof. Administration may be oral or intravenous. The medium chain triglycerides may be emulsified, and may be coadministered with L-carnitine or a derivative of L-carnitine.

SUMM [0027] The present invention also provides a method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of free fatty acids derived from medium chain triglycerides to a patient in need thereof.

SUMM [0028] The present invention also provides a method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of a medium chain triglyceride prodrug to a patient in need thereof.

SUMM [0029] The present invention also provides a method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of a therapeutic agent which induces utilization of fatty acids and development of ketosis to a patient in need thereof.

SUMM [0030] The present invention further provides therapeutic agents for the treatment or prevention of dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism.

DETD [0032] The background of this invention supports the present invention in the following ways. (1) Neurons of the brain can use both glucose and ketone bodies for respiration. (2) The neurons of **Alzheimer**'s Disease patients have well documented defects in glucose metabolism. (3) Known genetic risk factors for **Alzheimer**'s Disease are associated with lipid and cholesterol transport, suggesting defects in triglyceride usage may underlie susceptibility to **Alzheimer**'s Disease. (4) A diet rich in MCT will lead to increased levels of blood ketone bodies and thereby provide energy to starving brain neurons. Hence, supplementation of **Alzheimer**'s Disease patients with MCT will restore neuronal metabolism.

DETD [0033] The present invention provides a method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of medium chain triglycerides to a patient in need thereof. Generally, an effective amount is an amount effective to either (1) reduce the symptoms of the disease sought to be treated or (2) induce a pharmacological change relevant to treating the disease sought to be treated. For **Alzheimer**'s Disease, an effective amount includes an amount effective to: increase cognitive scores; slow the progression of dementia; or increase the life expectancy of the affected patient. As used herein, medium chain triglycerides of this invention are represented by the following formula:

DETD [0036] In another preferred embodiment, the invention provides a method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of free fatty acids, which may be derived from medium chain triglycerides, to a patient in need thereof. Such fatty acids are referred to herein as free medium chain fatty acids, or free fatty acids. Because MCT are metabolized to produce medium chain fatty acids, which are oxidized, the administration of free fatty acids and/or ketone bodies have the same effect as the administration of MCT themselves.

DETD [0037] In another preferred embodiment, the invention comprises the coadministration of emulsified tri-C6:0 MCT and L-camitine or a derivative of Lcamitine. Slight increases in MCFA oxidation have been noted when MCT are combined with L-camitine (Odle, 1997). Thus in the present invention emulsified triC6:0 MCT are combined with L-camitine at doses required to increase the utilization of said MCT. The dosage of L-camitine and MCT will vary according to the condition of the host, method of delivery, and other factors known to those skilled in the art, and will be of sufficient quantity to raise blood ketone levels to a degree required to treat and prevent **Alzheimer**'s Disease. Derivatives of L-camitine which may be used in the present invention include but are not limited to decanoylcamitine, hexanoylcamitine, caproylcarnitine, lauroylcarnitine, octanoylcatnitine, stearoylcarnitine, myristoylcamitine, acetyl-L-carnitine, O-Acetyl-L-carnitine, and palmitoyl-L-carnitine.

DETD [0040] Oral and intravenous administration of MCT or fatty acids result in hyperketonemia. Hyperketonemia results in ketone bodies being utilized for energy in the brain even in the presence of glucose. Additionally, hyperketonemia results in a substantial (39%) increase in cerebral blood flow (Hasselbalch et al. 1996). Hyperketonemia has been

reported to reduce cognitive dysfunction associated with systemic hypoglycemia in normal humans (Veneman et al. 1994). Please note that systemic hypoglycemia is distinct from the local defects in glucose metabolism that occur in AD. In another embodiment, the invention provides the subject compounds in the form of one or more prodrugs, which can be metabolically converted to the subject compounds by the recipient host. As used herein, a prodrug is a compound that exhibits pharmacological activity after undergoing a chemical transformation in the body. The said prodrugs will be administered in a dosage required to increase blood ketone bodies to a level required to treat and prevent the occurrence of **Alzheimer**'s Disease. A wide variety of prodrug formulations are known in the art. For example, prodrug bonds may be hydrolyzable, such as esters or anhydrides, or enzymatically biodegradable, such as amides.

DETD [0041] This invention also provides a therapeutic agent for the treatment or prevention of dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising medium chain triglycerides. In a preferred embodiment, the therapeutic agent is provided in administratively convenient formulations of the compositions including dosage units incorporated into a variety of containers. Dosages of the MCT are preferably administered in an effective amount, in order to produce ketone body concentrations sufficient to increase the cognitive ability of patients afflicted with AD or other states of reduced neuronal metabolism. For example, for the ketone body D-beta-hydroxybutyrate, blood levels are raised to about 1-10 mM or as measured by urinary excretion in the range of about 5 mg/dL to about 160 mg/dL, although variations will necessarily occur depending on the formulation and host, for example. Effective amount dosages of other MCTs will be apparent to those skilled in the art. Convenient unit dosage containers and/or formulations include tablets, capsules, lozenges, troches, hard candies, nutritional bars, nutritional drinks, metered sprays, creams, and suppositories, among others. The compositions may be combined with a pharmaceutically acceptable excipient such as gelatin, an oil, and/or other pharmaceutically active agent(s). For example, the compositions may be advantageously combined and/or used in combination with other therapeutic or prophylactic agents, different from the subject compounds. In many instances, administration in conjunction with the subject compositions enhances the efficacy of such agents. For example, the compounds may be advantageously used in conjunction with antioxidants, compounds that enhance the efficiency of glucose utilization, and mixtures thereof, (see e.g. Goodman et al. 1996).

DETD [0042] In a preferred embodiment the human subject is intravenously infused with MCT, MCFA (medium chain fatty acids) and/or ketone bodies directly, to a level required to treat and prevent the occurrence of **Alzheimer**'s Disease. Preparation of intravenous lipid, and ketone body solutions is well known to those skilled in the art.

DETD [0045] In another embodiment, the invention provides the recipient with a therapeutic agent which enhances endogenous fatty acid metabolism by the recipient. The said therapeutic agent will be administered in a dosage required to increase blood ketone bodies to a level required to treat and prevent the occurrence of **Alzheimer**'s Disease.
Ketone bodies are produced continuously by oxidation of fatty acids in tissues that are capable of such oxidation. The major organ for fatty acid oxidation is the liver. Under normal physiological conditions ketone bodies are rapidly utilized and cleared from the blood. Under some conditions, such as starvation or **low carbohydrate diet**, ketone bodies are produced in excess and accumulate in the blood stream. Compounds that mimic the effect of increasing oxidation of fatty acids will raise ketone body concentration to a level to provide an alternative energy source for neuronal cells with compromised metabolism. Since the efficacy of such compounds derives from their ability to increase fatty acid utilization and raise blood ketone body concentration they are dependent on the

embodiments of the present invention.

DETD [0046] From the description above, a number of advantages of the invention for treating and preventing **Alzheimer**'s Disease become evident:

DETD [0052] Accordingly, the reader will see that the use of medium chain triglycerides (MCT) or fatty acids as a treatment and preventative measure of **Alzheimer**'s Disease (AD) provides a novel means of alleviating reduced neuronal metabolism associated with AD. It is the novel and significant insight of the present invention that use of MCT results in hyperketonemia which will provide increased neuronal metabolism for diseases associated with reduced neuronal metabolism, such as AD, ALS, Parkinson's Disease and Huntington's Disease. Although the description above contains many specificities, these should not be construed as limiting the scope of the invention but merely as providing illustrations for some of the presently preferred embodiments of this invention. For example, supplementation with MCT may prove more effective when combined with insulin sensitizing agents such as vanadyl sulfate, chromium picolinate, and vitamin E. Such agents may function to increase glucose utilization in compromised neurons and work synergistically with hyperketonemia. In another example MCT can be combined with compounds that increase the rates of fatty acid utilization such as L-camitine and its derivatives. Mixtures of such compounds may synergistically increase levels of circulating ketone bodies.

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and Stadlan, E. M. (1984). Clinical diagnosis of **Alzheimer**'s disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on **Alzheimer**'s Disease. Neurology 34:939-44.

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DETD [0094] Swaab, D. F., Lucassen, P. J., Salehi, A., Scherder, E. J., van Someren, E. J., and Verwer, R. W. (1998) Reduced neuronal activity and reactivation in **Alzheimer**'s disease. Prog Brain Res 117:343-77.

DETD [0097] Zubenko, G. S., Stiffler, J. S., Hughes, H. B., and Martinez, A. J. (1999) Reductions in brain phosphatidylinositol kinase activities in **Alzheimer**'s disease. Biol Psychiatry 45:731-6.

CLM What is claimed is:

1. A method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of medium chain triglycerides to a patient in need thereof.

10. A method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of free medium chain fatty acids.

11. A method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of a medium chain triglyceride prodrug to a patient in need thereof.

12. A method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of a therapeutic agent which induces utilization of fatty acids and development of ketosis to a patient in need thereof.

13. A method of treating or preventing dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising coadministering an effective amount of an agent selected from the group consisting of medium chain triglycerides, medium chain fatty acids, and ketone bodies, and Lcamitine or a derivative of L-camitine to a patient in need thereof.

16. A therapeutic agent for the treatment of prevention or dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism comprising medium chain triglycerides.

17. A therapeutic agent for the treatment of prevention or dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism comprising free fatty acids derived from medium chain triglycerides .

18. A therapeutic agent for the treatment of prevention or dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism comprising a medium chain triglyceride prodrug.

19. A therapeutic agent for the treatment of prevention or dementia of **Alzheimer**'s type, or other loss of cognitive function caused by reduced neuronal metabolism comprising an agent which induces utilization of fatty acids and development of ketosis to a patient in need thereof.

ACCESSION NUMBER: 2002:12577 USPATFULL
TITLE: Use of medium chain triglycerides for the treatment and prevention of **Alzheimer**'s Disease and other diseases resulting from reduced Neuronal Metabolism
INVENTOR(S): Henderson, Samuel T., Broomfield, CO, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002006959	A1	20020117
APPLICATION INFO.:	US 2001-845741	A1	20010501 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-200980P	20000501 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SWANSON & BRATSCHUN L.L.C., 1745 SHEA CENTER DRIVE, SUITE 330, HIGHLANDS RANCH, CO, 80129
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 1
LINE COUNT: 936
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L51 ANSWER 5 OF 12 USPATFULL
SUMM A large number of pharmacological agents that affect behavior is known. Perhaps one of the best known is the combination Fen-Phen used for many years to exert an anorectic effect to treat obesity. This combination of phentermine and fenfluramine was available until recently when the cardiopulmonary side effects of this medicament were considered unacceptable. Both of these components are related to amphetamines and are epinephrine analogs which can be used to combat fatigue and drowsiness. The use of, for example, donepezil to treat the symptoms of **Alzheimer**'s disease is also known. In short, a variety of agents known to affect the central nervous system have been used in various contexts to treat a number of indications related directly or indirectly to behaviors.

DETD This gentleman has been a patient in this practice for many years. His medical problems are extremely long-lived and include chronic depression, severe obesity, hypertension, stasis dermatitis, and venous insufficiency of the lower extremities, and seborrhea. His depression was related historically to the fact that he was adopted and has never developed a good sense of self. His bilateral stasis dermatitis from chronic thrombophlebitis was very severe and interrupted his work on a frequent basis. He was 5'81/2" tall and frequently unmeasurable at over 350 lb. Various attempts to get weight off him were successful, but none on a consistent basis. Sleep apnea was diagnosed and he was using a CPAP mask, high protein/**low carbohydrate diets** were mildly successful with approximately a 30 or 40 lb weight loss but they did not hold. The patient would occasionally become disillusioned with therapy and his physicians and withdraw, but would eventually return.

ACCESSION NUMBER: 2001:235278 USPATFULL
TITLE: Behavior chemotherapy
INVENTOR(S): Eig, Mark H., Chevy Chase, MD, United States
PATENT ASSIGNEE(S): Be Able, LLC, Chevy Chase, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6333357	B1	20011225	
APPLICATION INFO.:	US 1999-434286		19991105	(9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Criares, Theodore J.
ASSISTANT EXAMINER: Kim, Jennifer
LEGAL REPRESENTATIVE: Morrison & Foerster LLP
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
LINE COUNT: 719
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ility of
insulin to exert its biological action across a broad range of concentrations. In **insulin resistance**, the body secretes abnormally high amounts of insulin to compensate for this defect; failing which, the plasma glucose concentration inevitably rises and develops into diabetes. Among the developed countries, diabetes mellitus is a common problem and is associated with a variety of abnormalities including obesity, hypertension, hyperlipidemia (J. Clin. Invest., (1985) 75: 809-817; N. Engl. J. Med.; (1987) 317: 350-357; J. Clin. Endocrinol. Metab., (1988) 66: 580-583; J. Clin. Invest., (1975) 68: 957-969) and other renal complications (See Patent Application No. WO 95/21608). It is now increasingly being recognized that **insulin resistance** and relative hyperinsulinemia have a contributory role in obesity, hypertension, atherosclerosis and type 2 diabetes mellitus. The association of **insulin resistance** with obesity, hypertension and angina has been described as a syndrome having **insulin resistance** as the central pathogenic link-Syndrome-X. In addition, polycystic ovarian syndrome (Patent Application No. WO 95/07697), psoriasis (Patent Application No. WO 95/35108), dementia (Behavioral Brain Research (1996) 75: 1-11) etc., may also have **insulin resistance** as a central pathogenic feature.

SUMM A number of molecular defects have been associated with **insulin resistance**. These include reduced expression of insulin receptors on the plasma membrane of insulin responsive cells and alterations in the signal transduction pathways that become activated after insulin binds to its receptor including glucose transport and glycogen synthesis.

SUMM The present invention also provides a pharmaceutical composition, containing the compounds of the general formula (I), as defined above, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates in combination with the usual pharmaceutically employed carriers, diluents and the like, useful for the treatment and/or prophylaxis of diseases in which **insulin resistance** is the underlying pathophysiological mechanism such as type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease and other cardiovascular disorders including atherosclerosis; **insulin resistance** associated with obesity and psoriasis, for treating diabetic complications and other diseases such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders, as aldose reductase inhibitors and for improving cognitive functions in dementia.

DETD Mutation in colonies of laboratory animals and different sensitivities to dietary regimens have made the development of animal models with non-insulin dependent diabetes associated with obesity and **insulin resistance** possible. Genetic models such as db/db and ob/ob (See Diabetes, (1982) 31(1): 1-6) in mice and fa/fa and zucker rats have been developed by the various laboratories for understanding the pathophysiology of disease and testing the efficacy of new antidiabetic compounds (Diabetes, (1983) 32: 830-838; Annu. Rep. Sankyo Res. Lab. (1994) 46: 1-57). The homozygous animals, C57 BL/KsJ-db/db mice developed by Jackson Laboratory, U.S., are obese, hyperglycemic, hyperinsulinemic and insulin resistant (J. Clin. Invest., (1990) 85:962-967), whereas heterozygous are lean and normoglycemic. In db/db model, mouse progressively develops insulinopenia with age, a feature commonly observed in late stages of human type II diabetes when blood sugar levels are insufficiently controlled. The state of pancreas

and its course vary according to the models. Since this model resembles that of type II diabetes mellitus, the compounds of the present invention were tested for blood sugar and triglycerides lowering activities.

DETD The compounds of the present inventions showed blood sugar and triglycerides lowering activities through improved **insulin resistance**. This was demonstrated by the following in vivo experiments.

CLM What is claimed is:

10. A method of preventing or treating diseases in which **insulin resistance** is the underlying pathophysiological mechanism comprising administering a compound of formula (I) as defined in claim 1, and a pharmaceutically acceptable carrier, diluent or excipient to a patient in need thereof.

11. A method according to claim 10, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease, cardiovascular disorders, atherosclerosis, **insulin resistance** associated with obesity and psoriasis, diabetic complications, polycystic ovarian syndrome (PCOS), renal diseases, diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases, microalbuminuria, eating disorders.

IT 121-33-5, Vanillin 123-08-0, 4-Hydroxybenzaldehyde **140-88-5** 491-36-1, 3,4-Dihydroquinazolin-4-one 1769-24-0 2295-31-0, Thiazolidine-2,4-dione 2346-24-9 3137-64-2 3282-30-2, Pivaloyl chloride 4141-08-6, o-Amino-N-methylbenzamide 6622-92-0 13288-06-7 14631-20-0 16673-85-1 16858-16-5 16858-50-7 18593-45-8 28279-12-1 52191-15-8, 4-(2-Bromoethoxy)benzaldehyde 52421-76-8 90565-51-8 179087-93-5 199114-61-9 221208-19-1 221208-20-4 221208-21-5
(prepn. of pyrimidinylethoxybenzylthiazolidinediones)

ACCESSION NUMBER: 1999:37111 USPATFULL

TITLE: Heterocyclic compounds, process for their preparation and pharmaceutical compositions containing them and their use in the treatment of diabetes and related diseases

INVENTOR(S): Lohray, Vidya Bhushan, Hyderabad, India
Lohray, Braj Bhushan, Hyderabad, India
Paraselli, Rao Bheema, Hyderabad, India

PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, Hyderabad, India (non-U.S. corporation)
Reddy-Cheminor, Inc., Ridgewood, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5885997		19990323
APPLICATION INFO.:	US 1996-777627		19961231 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	IN 1996-115096	19960701

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose G.
ASSISTANT EXAMINER: Oazi, Sabiha N.
LEGAL REPRESENTATIVE: Ladas & Parry
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
LINE COUNT: 1914
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L74 ANSWER 22 OF 23 USPATFULL

SUMM The thiazolidinedione derivatives of the general formula (I) defined above of the present invention are useful for the treatment and/or prophylaxis of diseases in which **insulin resistance** is the underlying pathophysiological mechanism such as type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease and other cardiovascular disorders including atherosclerosis, **insulin resistance** associated with obesity and psoriasis; for treating diabetic complications and other diseases such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders; as aldose reductase inhibitors and for improving cognitive functions in dementia.

y acceptable
solvates in combination with the usual pharmaceutically employed carriers, diluents and the like. The thiazolidinedione derivatives of the general formula (I) defined above of the present invention are useful for the treatment and/or prophylaxis of diseases in which **insulin resistance** is the underlying pathophysiological mechanism such as type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease and other cardiovascular disorders including atherosclerosis, **insulin resistance** associated with obesity and psoriasis; for treating diabetic complications and other diseases such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders; as aldose reductase inhibitors and for improving cognitive functions in dementia. The pharmaceutical composition may be in the forms normally employed, such as tablets, capsules, powders, syrups, solutions, suspensions and the like, may contain flavorants, sweeteners etc. in suitable solid or liquid carriers or diluents, or in suitable sterile media to form injectable solutions or suspensions. Such compositions typically contain from 1 to 20%, preferably 1 to 10% by weight of active compound, the remainder of the composition being pharmaceutically acceptable carrier, diluent or solvent.

DETD The compounds of the present invention showed blood sugar and triglycerides lowering activites through improving **insulin resistance** which has been demonstrated by the following in vivo experiment.

CLM What is claimed is:

20. A pharmaceutical composition for the treatment or prophylaxis of diseases in which **insulin resistance** is the underlying pathophysiological mechanism such as type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease and other cardiovascular disorders including atherosclerosis, **insulin resistance** associated with obesity and psoriasis, for treating diabetic complications and other diseases such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders, as aldose reductase inhibitors and for improving cognitive functions in dementia, which comprises a compound of the formula (I) as defined in claim 1, together with pharmaceutically acceptable carriers, diluents, or solvates.

22. A method for preventing or treating diseases in which **insulin resistance** is underlying pathophysiological mechanism comprising administering a compound of formula (I) as defined in claim 1, and a pharmaceutically acceptable carrier, diluent or solvate to a patient in need thereof.

23. A method according to claim 22, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease, a cardiovascular disorder, atherosclerosis, **insulin resistance** associated with obesity and psoriasis, diabetic complications, polycystic ovarian syndrome (PCOS), renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases, microalbuminuria, or eating disorders.

25. A pharmaceutical composition for the treatment or prophylaxis of diseases in which **insulin resistance** is the underlying pathophysiological mechanism such as type II diabetes,

impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease and other cardiovascular disorders including atherosclerosis, **insulin resistance** associated with obesity and psoriasis, for treating diabetic complications and other diseases such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders, as aldose reductase inhibitors and for improving cognitive functions in dementia, which comprises a compound of the formula (a) as defined in claim 24, together with pharmaceutically acceptable carriers, diluents, or solvates.

27. A method for preventing or treating diseases in which **insulin resistance** is underlying pathophysiolocial mechanism comprising administering a compound of formula (I) as defined in claim 24, and a pharmaceutically acceptable carrier, diluent or solvate to a patient in need thereof.

28. A method according to claim 27, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipideamia, hypertension, coronary heart disease, a cardiovascular disorder, atherosclerosis, **insulin resistance** associated with obesity and psoriasis, diabetic complications, polycystic ovarian syndrome (PCOS), renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases, microalbuminuria, or eating disorders.

IT 62-56-6, Thiourea, reactions 109-09-1, 2-Chloropyridine 123-08-0, 4-Hydroxybenzaldehyde 124-63-0, Methanesulfonyl chloride **140-88-5** 350-46-9, 1-Fluoro-4-nitrobenzene 459-57-4, 4-Fluorobenzaldehyde 612-62-4, 2-Chloroquinoline 634-47-9, 2-Chlorolepidine 2295-31-0, 2,4-Thiazolidinedione 5382-16-1, 4-Piperidinol 6457-49-4, 4-Hydroxymethylpiperidine 23356-96-9, L-Prolinol 100243-39-8, (S)-3-Pyrrolidinol 103003-01-6, 2-Hydroxymethylmorpholine 199118-03-1 199118-05-3
(for prepn. of thiazolidinediones having antidiabetic, hypolipidemic and antihypertensive properties)

ACCESSION NUMBER: 1998:104743 USPATFULL

TITLE: Heterocyclic compounds having antidiabetic, hypolipidaemic, antihypertensive properties, process for their preparation and pharmaceutical compositions containing them

INVENTOR(S): Lohray, Vidya Bhushan, Hyderabad, India
Lohray, Braj Bhushan, Hyderabad, India
Alla, Sekar Reddy, Hyderabad, India
Ramanujam, Rajagopalan, Hyderabad, India
Chakrabarti, Ranjan, Hyderabad, India

PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, Hyderabad, India (non-U.S. corporation)
Reddy-Cheminor, Inc., Ridgewood, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5801173		19980901
APPLICATION INFO.:	US 1996-687840		19960726 (8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gerstl, Robert
LEGAL REPRESENTATIVE: Ladas & Parry
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1

LINE COUNT: 1138
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

EXEMPLARY CLAIM: 1
LINE COUNT: 2164
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L74 ANSWER 18 OF 23 USPATFULL

SUMM The thiazolidinedione derivatives of the general formula (I) defined above of the present invention are useful for the treatment and/or prophylaxis of diseases or conditions in which **insulin resistance** is the underlying pathophysiological mechanism. Examples of these diseases and conditions are type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease and other cardiovascular disorders including atherosclerosis. The thiazolidinedione derivatives of the formula (I) are useful for the treatment of **insulin resistance** associated with obesity and psoriasis. The thiazolidinedione derivatives of the formula (I) can also be used to treat diabetic complications and can be used for treatment and/or prophylaxis of other diseases and conditions such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders, as aldose reductase inhibitors and for improving cognitive functions in dementia.

SUMM **Insulin resistance** is the diminished ability of insulin to exert its biological action across a broad range of concentrations. In **insulin resistance**, the body secretes abnormally high amounts of insulin to compensate for this defect; failing which, the plasma glucose concentration inevitably rises and develops into diabetes. Among the developed countries, diabetes mellitus is a common problem and is associated with a variety of abnormalities including obesity, hypertension, hyperlipidemia (J. Clin. Invest., (1985) 75: 809-817; N. Engl. J. Med. (1987) 317: 350-357; J. Clin. Endocrinol. Metab., (1988) 66: 580-583; J. Clin. Invest., (1975) 68: 957-969) and other renal complications (See Patent Application No. WO 95/21608). It is now increasingly being recognized that **insulin resistance** and relative hyperinsulinemia have a contributory role in obesity, hypertension, atherosclerosis and type 2 diabetes mellitus. The association of **insulin resistance** with obesity, hypertension and angina has been described as a syndrome having **insulin resistance** as the central pathogenic link-Syndrome-X. In addition, polycystic ovarian syndrome (Patent Application No. WO 95/07697), psoriasis (Patent Application No. WO 95/35108), dementia (Behavioral Brain Research (1996) 75: 1-11) etc. may also have **insulin resistance** as a central pathogenic feature.

SUMM A number of molecular defects have been associated with **insulin resistance**. These include reduced expression of insulin receptors on the plasma membrane of insulin responsive cells and alterations in the signal transduction pathways that become activated after insulin binds to its receptor including glucose transport and glycogen synthesis.

DETD The present invention also provides a pharmaceutical composition, containing the compounds of the general formula (I), as defined above, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates in combination with the usual pharmaceutically employed carriers, diluents and the like, useful for the treatment and/or prophylaxis of diseases in which **insulin resistance** is the underlying pathophysiological mechanism such as type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart

disease and other cardiovascular disorders including atherosclerosis; **insulin resistance** associated with obesity and psoriasis, for treating diabetic complications and other diseases such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders, as aldose reductase inhibitors and for improving cognitive functions in dementia.

DETD Mutation in colonies of laboratory animals and different sensitivities to dietary regimens have made the development of animal models with non-insulin dependent diabetes associated with obesity and **insulin resistance** possible. Genetic models such as db/db and ob/ob (See Diabetes, (1982) 31(1): 1-6) in mice and fa/fa and zucker rats have been developed by the various laboratories for understanding the pathophysiology of disease and testing the efficacy of new antidiabetic compounds (Diabetes, (1983) 32: 830-838; Annu. Rep. Sankyo Res. Lab. (1994). 46: 1-57). The homozygous animals, C57 BL/KsJ-db/db mice developed by Jackson Laboratory, US, are obese, hyperglycemic, hyperinsulinemic and insulin resistant (J. Clin. Invest., (1990) 85: 962-967), whereas heterozygous are lean and normoglycemic. In db/db model, mice progressively develop insulinopenia with age, a feature commonly observed in late stages of human type II diabetes when blood sugar levels are insufficiently controlled. The state of pancreas and its course vary according to the models. Since this model resembles that of type II diabetes mellitus, the compounds of the present invention were tested for blood sugar and triglycerides lowering activities.

DETD The compounds of the present invention showed blood sugar and triglycerides lowering activities through improved **insulin resistance**. This was demonstrated by the following in vivo experiments.

CLM What is claimed is:

21. A pharmaceutical composition useful for the treatment and/or prophylaxis of diseases in which **insulin resistance** is the underlying pathophysiological mechanism such as type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease and other cardiovascular disorders including atherosclerosis, **insulin resistance** associated with obesity and psoriasis, for treating diabetic complications and other diseases such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders, as aldose reductase inhibitors and for improving cognitive functions in dementia, which comprises a compound of the general formula (I) as defined in claim 1, together with pharmaceutically acceptable carriers, diluents, or solvates.

24. A method of preventing or treating diseases in which **insulin resistance** is the underlying pathophysiological mechanism comprising administering a compound of formula (I) as defined in claim 1, and a pharmaceutically acceptable carrier, diluent or solvate to a patient in need thereof.

27. A method according to claim 24, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease, a cardiovascular disorder, atherosclerosis, **insulin resistance** associated with obesity and psoriasis, diabetic complications, polycystic ovarian syndrome (PCOS), renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases, microalbuminuria, or eating disorders or dementia.

IT 62-56-6, Thiourea, reactions 109-09-1, 2-Chloropyridine 123-08-0, 4-Hydroxybenzaldehyde 124-63-0, Methanesulfonyl chloride **140-88-5** 350-46-9, 1-Fluoro-4-nitrobenzene 459-57-4, 4-Fluorobenzaldehyde 612-62-4, 2-Chloroquinoline 634-47-9, 2-Chlorolepidine 2295-31-0, 2,4-Thiazolidinedione 5382-16-1, 4-Piperidinol 6457-49-4, 4-Hydroxymethylpiperidine 23356-96-9, L-Prolinol 100243-39-8, (S)-3-Pyrrolidinol 103003-01-6, 2-Hydroxymethylmorpholine 199118-03-1 199118-05-3
(for prepn. of thiazolidinediones having antidiabetic, hypolipidemic and antihypertensive properties)

ACCESSION NUMBER: 1999:75638 USPATFULL

TITLE: Heterocyclic compounds having antidiabetic, hypolipidaemic, antihypertensive properties, process for their preparation and pharmaceutical compositions containing them

INVENTOR(S): Lohray, Vidya Bhushan, Hyderabad, India
Lohray, Braj Bhushan, Hyderabad, India
Rao, Paraselli Bheema, Hyderabad, India
Alla, Sekar Reddy, Hyderabad, India
Ramanujam, Rajagopalan, Hyderabad, India
Chakrabarti, Ranjan, Hyderabad, India

PATENT ASSIGNEE(S): Dr. Reddy's Research Foundation, Hyderabad, India (non-U.S. corporation)
Reddy-Cheminor, Inc., Ridgewood, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5919782		19990706
APPLICATION INFO.:	US 1997-851447		19970505 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-687840, filed on 26 Jul 1996, now patented, Pat. No. US 5801173

	NUMBER	DATE
PRIORITY INFORMATION:	IN 1996-72396	19960506

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Gerstl, Robert
LEGAL REPRESENTATIVE: Ladas & Parry
NUMBER OF CLAIMS: 27

L21 ANSWER 8 OF 9 USPATFULL

DETD After the staining solution is combined with a sample, sufficient time is allowed for the dye in the solution to stain cells in the sample so that formation of distinct intravacuolar structures (DIS) can be evaluated. Typically, more than about 10 or 15 minutes is sufficient time for the dye to stain cells in the sample. More typically, the dye solution is combined with the sample for more than about 30 minutes. Practically instantaneous generation of DIS is achieved when a **metabolizable carbohydrate** is added to cells for which the metabolism is previously suppressed. The cells are **treated** overnight with a non-metabolizable substrate (e.g. 2% 2-deoxyglucose containing 0.5% sodium azide). After washing the cells free of the substrate, the cells are stained with the subject dyes. Very few if any DIS appear even after an hour of incubation, but appear virtually instantaneously when a **metabolizable carbohydrate** (e.g. 2% glucose and 10 mM HEPES) is added to the cell medium.

ACCESSION NUMBER: 95:78086 USPATFULL

TITLE: Intravacuolar stains for yeast and other fungi

INVENTOR(S): Roth, Bruce L., Corvallis, OR, United States
Millard, Paul J., Eugene, OR, United States
Yue, Stephen T., Eugene, OR, United States
Haugland, Richard P., Eugene, OR, United States

PATENT ASSIGNEE(S): Molecular Probes, Inc., Eugene, OR, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5445946		19950829
APPLICATION INFO.:	US 1994-206081		19940303 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1993-90890, filed on 12 Jul 1993 whic		

SUMM In the preparation of various foodstuffs and other ingested items, such as vitamins, drugs and the like, such foodstuffs having been encapsulated to provide a delayed release flavor, medicinal action or the like. As stated above, the subject invention relates to an encapsulated and coated **metabolizable carbohydrate** composition which has a controlled release upon ingestion whereby the carbohydrates are slowly released into the body's digestive tract. This delayed release action can be very helpful in counteracting the effects of diseases, such as diabetes which is characterized by a raised glucose concentration in the blood due to a deficiency or diminished effectiveness of insulin. The disease is chronic and also affects the metabolism of fat and protein. In general, some cases can be controlled by **diet** alone while others require **diet** and insulin, and for still others control with drugs is needed.

ACCESSION NUMBER: 96:72660 USPATFULL

TITLE: Method of controlling the release of carbohydrates by encapsulation and composition therefor

INVENTOR(S): Fox, J. Gary, Princeton Junction, NJ, United States
Allen, Darlene, Berkeley Heights, NJ, United States

PATENT ASSIGNEE(S): The Estee Corporation, Parsippany, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5545410		19960813
APPLICATION INFO.:	US 1994-331671		19941031 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-53944, filed on 26 Apr 1993, now patented, Pat. No. US 5360614, issued on 1 Nov 1994

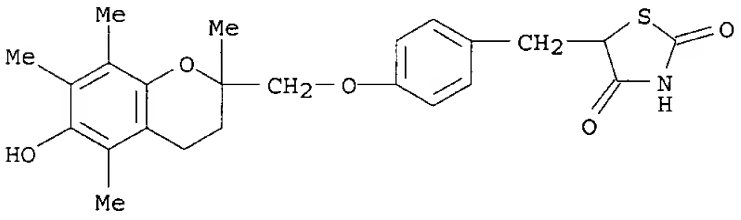
L30 ANSWER 5 OF 9 USPATFULL

SUMM In the preparation of various foodstuffs and other ingested items, such as vitamins, drugs and the like, such foodstuffs having been encapsulated to provide a delayed release flavor, medicinal action or the like. As stated above, the subject invention relates to an encapsulated and coated **metabolizable carbohydrate** composition which has a controlled release upon ingestion whereby the carbohydrates are slowly released into the body's digestive tract. This delayed release action can be very helpful in counteracting the effects of diseases, such as diabetes which is characterized by a raised glucose concentration in the blood due to a deficiency or diminished effectiveness of insulin. The disease is chronic and also affects the metabolism of fat and protein. In general, some cases can be controlled by **diet** alone while others require **diet** and insulin, and for still others control with drugs is needed.

ACCESSION NUMBER:	94:95228 USPATFULL
TITLE:	Method of controlling the release of carbohydrates by encapsulation and composition therefor
INVENTOR(S):	Fox, J. Gary, Princeton Junction, NJ, United States Allen, Darlene, Berkeley Heights, NJ, United States
PATENT ASSIGNEE(S):	The Estee Corporation, Parsippany, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5360614		19941101	
APPLICATION INFO.:	US 1993-53944		19930426	(8)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Phelan, D. Gabrielle			
ASSISTANT EXAMINER:	Azpuru, Carlos			
LEGAL REPRESENTATIVE:	Welsh & Katz, Ltd.			
NUMBER OF CLAIMS:	4			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)			
LINE COUNT:	499			

L188 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN **97322-87-7** REGISTRY
CN 2,4-Thiazolidinedione, 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 58: PN: WO0148150 SEQID: 73 claimed sequence
CN CI 991
CN CS 045
CN GR 92132X
CN Noscal
CN Rezulin
CN Romglizone
CN Troglitazone
FS 3D CONCORD
DR 259223-65-9
MF C24 H27 N O5 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

915 REFERENCES IN FILE CA (1962 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
924 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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Connection closed by remote host

L6 ANSWER 19 OF 21 USPATFULL

SUMM In normal aging, the brain loses neurons, including those that are dependent on the **diet** and blood stream for the precursors of their neurotransmitters, for example, acetylcholine-releasing or "cholinergic" neurons, which make acetylcholine from dietary lecithin or circulating choline; "catecholaminergic" neurons, that make dopamine, norepinephrine, or epinephrine from tyrosine; "serotoninergic" neurons, that synthesize serotonin from tryptophan; or "glycinergic" neurons, that can produce glycine from the amino acid threonine. Neuronal cell loss is specifically exacerbated in particular neurological diseases, such as senility or **Alzheimer**'s Disease in which cholinergic neurons are especially deficient, but catecholaminically affects dopaminergic neurons. Unfortunately, there is no presently available means to determine in a particular normal old person, or a person with a neurological disease, how many of which neuronal types have been lost. Moreover, a **treatment** that replaces one of the deficient neurotransmitters might be of limited utility if another transmitter were also deficient. Ideally, a **treatment** for this neuronal loss would provide the brain with agents that could increase the synthesis and release any of several transmitters, but which would have an effect only if each transmitter's release were deficient.

SUMM It is known that giving experimental animals choline enhances acetylcholine synthesis in rapidly-firing cholinergic neurons, and therefore is useful in treating disease states characterized by inadequate acetylcholine release, for example, Alzheimer's Disease, in which the surviving neurons presumably fire frequently, to make up for the missing ones, and also as a supplement to drugs which either act by releasing acetylcholine or which, as a side-effect, deplete neurons of acetylcholine. It is also known that giving tyrosine similarly enhances catecholamine release from rapidly-firing neurons, and that giving tryptophan or threonine enhances serotonin or glycine production in serotoninergic or glycinergic neurons, respectively. It is also known that the effectiveness of giving any of these amino acids can be potentiated by providing the amino acid in the proper ratio to **carbohydrates** which elicit insulin secretion, and which thereby lower plasma levels of other amino acids that compete with the desired one for uptake into the brain.

SUMM In the process of this invention, the choline or compound that dissociates to choline is administered concomitantly with the amino acid. The administration of the compositions employed in the present invention can be effected orally, interperitoneally, subcutaneously, intravenously or intramuscularly; the amino acids, tyrosine or tyrosine precursor (phenylalanine), threonine or tryptophan, can be used as such, as salts or esters, as peptides or as compounds which are metabolized to give the amino acids in vivo (e.g., alpha-keto amino acids). Conveniently, the compositions employed in this invention are admixed or dissolved in any innocuous vehicle such as water or sterile saline solution or in tablet or powder form containing the usual solid diluents or carriers, or as foods or enteral nutrition mixtures. The compositions employed in the present invention are administered in concentrations to avoid undesirable side effects. In humans, useful dosages of tyrosine are between about 0.5 mg/kg and 250 mg/kg (depending on route of administration), preferably between about 0.5 mg/kg and 50 mg/kg when given intravenously and 10 mg/kg and 200 mg/kg when given orally. (Threonine and tryptophan doses are similar). The administration of tyrosine or phenylalanine should, if possible, be made in the absence of other amino acids that might compete for uptake in the brain and which themselves do not produce dopamine. When tryptophan is administered, it can be administered with caffeine or another mild stimulant to suppress its effect on sleepiness. Also, the amino acid can be administered with an insulin-releasing **carbohydrate** such as sucrose, glucose or

L105 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 1998:320318 CAPLUS
DN 129:62740
TI Troglitazone: an antidiabetic agent
AU Chen, Connie
CS University HealthSystem Consortium, Oak Brook, IL, 60523, USA
SO American Journal of Health-System Pharmacy (1998), 55(9), 905-925
CODEN: AHSPEK; ISSN: 1079-2082
PB American Society of Health-System Pharmacists
DT Journal
LA English
CC 1-10 (Pharmacology)
AB The pharmacol., pharmacokinetics, clin. efficacy, adverse effects, and dosage and administration of troglitazone are reviewed. Troglitazone is the first oral thiazolidinedione approved for use in treating non-insulin-dependent diabetes mellitus (NIDDM). The drug's mechanism of action has not been fully elucidated. Troglitazone acts as an insulin sensitizer. Cell-line and animal models indicate that troglitazone may decrease hepatic glucose output by decreasing the rate of gluconeogenesis in the liver or by increasing glycolysis. Troglitazone is rapidly absorbed after oral administration, with peak concn. occurring in two to three hours. Food increases absorption by 30-85%. The drug is extensively metabolized in the liver. Troglitazone has been shown to be efficacious in treating NIDDM, both as monotherapy and in combination with oral sulfonylureas. Patients who are obese or who have **high** fasting plasma **insulin levels** may derive the greatest benefit. Patients with impaired glucose tolerance, syndrome X, polycystic ovary syndrome, gestational diabetes, or Werner's syndrome may also benefit from troglitazone. Adverse effects, including hematol. abnormalities, liver toxicity, and hypoglycemia, have been rare in published trials; no life-threatening effects have been reported thus far. The recommended initial dosage is 200 mg once daily with meals, with an increase to 400 mg daily if satisfactory glycemic control is not achieved after two to four weeks. The av. wholesale price is $348 for 100 200-mg tablets and $534 for 100 400-mg tablets. Troglitazone may be an effective agent for treating NIDDM, esp. in patients who are obese or who have **high** fasting plasma **insulin levels**.
ST troglitazone antidiabetic
IT Antidiabetic agents
(troglitazone as an antidiabetic agent in humans)
IT **97322-87-7**, Troglitazone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); **USES (Uses)**
(troglitazone as an antidiabetic agent in humans)

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L150 ANSWER 15 OF 19 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 95058391 EMBASE
DN 1995058391
TI Clinical pharmacology and therapeutics.
AU Breckenridge A.
CS Dept. Pharmacology and Therapeutics, University of Liverpool,Liverpool L69 3BX, United Kingdom
SO British Medical Journal, (1995) 310/6976 (377-380).
ISSN: 0959-8146 CODEN: BMJOAE
CY United Kingdom
DT Journal; Article
FS 030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
CT Medical Descriptors:
*clinical pharmacology
acquired immune deficiency syndrome: DT, drug therapy
alzheimer disease: DT, drug therapy
article
cost effectiveness analysis
degenerative disease: DT, drug therapy
diabetes mellitus: DT, drug therapy
good clinical practice
heart infarction: DT, drug therapy
human
labor inhibition
liver toxicity: SI, side effect
priority journal
Drug Descriptors:
alteplase: DT, drug therapy
apolipoprotein e4: EC, endogenous compound
captopril: DT, drug therapy
cerebrolysin: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
enalapril: DT, drug therapy
indometacin: DT, drug therapy
lisinopril: DT, drug therapy
nitric oxide
ramipril: DT, drug therapy
selegiline: DT, drug therapy
streptokinase: DT, drug therapy
tacrine: AE, adverse drug reaction
tacrine: TO, drug toxicity
tacrine: DT, drug therapy
troglitazone: DT, drug therapy
zidovudine: DT, drug therapy
RN (alteplase) 105857-23-6; (captopril) 62571-86-2; (cerebrolysin) 12656-61-0; (enalapril) 75847-73-3; (indometacin) 53-86-1, 74252-25-8, 7681-54-1; (lisinopril) 76547-98-3, 83915-83-7; (nitric oxide) 10102-43-9; (ramipril) 87333-19-5; (selegiline) 14611-51-9, 14611-52-0, 2079-54-1, 2323-36-6; (streptokinase) 9002-01-1; (tacrine) 1684-40-8, 3198-41-2, 321-64-2; (**troglitazone**) **97322-87-7**; (zidovudine) 30516-87-1

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